POSTER SESSION

1050 Prognostic Features in Stable Angina Pectoris

Sunday, March 30, 2003, 3:00 p.m.-5:00 p.m.
McCormick Place, Hall A
Presentation Hour: 3:00 p.m.-4:00 p.m.

1050-100 Prediction of Major Coronary Events in Stable Angina: The IONA Study

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Background: The Impact Of Nicorandil in Angina study ***(IONA)*** was a randomized controlled trial in 5126 patients with stable angina. Nicorandil, a potassium channel activator, reduced the incidence of the primary end point (CHD death, non fatal MI or unplanned hospitalization for angina) by 17%, HR 0.83 (0.72, 0.97), p = 0.014 and is the first anti anginal agent to be shown to improve clinical outcome in stable angina.
Methods: We interrogated the IONA database to identify factors related to outcome in order to inform clinical decision making about prognosis. Candidate factors were age, gender, Canadian Cardiovascular Society Functional status (CCSF), smoking, systolic blood pressure (SBP), heart rate, body mass index and histories of myocardial infarction, coronary artery bypass grafting (CABG), hypertension, diabetes, left ventricular hypertrophy on EKG and left ventricular systolic dysfunction. These were entered into a Cox proportional hazards model.
Results: All risk factors with the exception of gender, SBP, CABG, diabetes and hypertension were univariate predictors of the primary end point. The strongest multivariate predictors of outcome were, in descending order of importance, CCSF score IV, HR 5.49 (3.10, 10.00), p < 0.001; CCSF score III, HR 2.13 (1.67, 2.71), p < 0.001; CCSF II, HR 1.25 (1.04, 1.51), p = 0.021; previous MI, HR 1.54 (1.30, 1.83), p < 0.001; current smoking, HR 1.32 (1.10, 1.60), p = 0.004; age, HR 1.05 (1.00, 1.11), p = 0.035; treatment with nicorandil, HR 0.82 (0.71, 0.95), p = 0.009.
Conclusions: In the presence of medication which reduces major coronary events the profile of risk factors in patients with stable angina changes considerably. Traditionally strong factors including previous CABG, male gender, hypertension and diabetes were no longer even univariately predictive of outcome. By far the strongest predictor was clinical severity of angina (CCSF score) while smoking and previous MI also remain independently though less predictive than symptoms. These data could have an important influence on clinical assignment of risk and therefore on future clinical practice.

1050-101 Cumulative Infectious Burden (but Not Any Single Past Infection) Is Interrelated With Traditional Risk Factors to Cause Coronary Artery Disease

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The causative role of past infections in the pathogenesis of coronary artery disease (CAD) is uncertain.
Methods: We evaluated 179 consecutive patients, admitted electively for coronary angiography, for traditional atherosclerotic risk factors, serologic markers for prior infections with Chlamydia pneumonia, Helicobacter pylori, Cytomegalovirus (CMV), Epstein-Barr virus (EBV), Mycoplasma pneumonia, Hepatitis A virus (HAV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), fibrinogen and ferritin. Patients underwent coronary angiography. Patients with CAD were compared to patients with angiograpicaly normal coronary arteries (NCA).
Results: Serologic markers of past infection with Chlamydia pneumonia (IgG, IgA) and serologic marker of past infection with Helicobacter pylori (IgG) were more prevalent in the CAD patients group compared to NCA patients. However, after adjustment for traditional risk factors none of the serologic markers for infectious agents remained an independent risk factor for CAD, while the cumulative effect of numerous past infections was found to progressively increase the risk for CAD. Having 3-4 positive serologic markers confers a risk for CAD of 7.5 (CI 1.4-39.1) compared having 0-2 serologic markers. Having more than 5 serologic markers was shown to confer an even greater risk for CAD (16.8; CI 2.8-99).
Conclusions: The cumulative infections burden rather than any specific infection is related to an increased risk of coronary artery disease, implying that increased inflammatory burden over long periods of time might contribute to the pathogenesis of ischemic heart disease.

1050-102 Relation of Testosterone With Inflammatory Cytokines in Men With Coronary Artery Disease

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Background: Various cytokines have been identified as mediating the inflammatory process of atherosclerosis. Testosterone is known to possess anti-inflammatory properties and has been suggested as a therapy for some inflammatory conditions. Men with coronary artery disease have reduced levels of testosterone. Animal studies suggest that androgens may retard the progression of atherosclerosis. The mechanism of benefit is unknown but could involve immune modulation. In this study, we examined the relation between circulating levels of testosterone and inflammatory cytokines in men with established coronary artery disease.
Methods: Seventy five men with angiographically proven coronary artery disease (≥ 70% stenosis in ≥ 1 coronary artery) were studied. Blood samples were taken between 8 and 9.30am. Serum was removed by centrifugation and stored at -80° C until assayed. Serum levels of total and bio-available testosterone were measured, together with the pro-inflammatory cytokines tumour necrosis factor-α (TNF), interleukin- (Il-) 1β and Il-6, and the anti-inflammatory cytokine Il-10. Comparisons were made between eugonadal men and those with total testosterone level ≤ 7.5nmol/L or bio-available testosterone ≤ 2.5nmol/L, using the Mann Whitney U test.
Results: Eighteen subjects had low androgen levels. Compared with eugonadal subjects, levels of Il-1β were significantly elevated (516 ± 127fg/ml *v* 253 ± 42fg/ml, p=0.030). Levels of TNF, Il-6 and Il-10 did not differ significantly between groups (TNF 2.59 ± 0.75pg/ml *v* 2.35 ± 0.34pg/ml, p=0.785; Il-6 3.58 ± 0.61pg/ml *v* 6.66 ± 2.72pg/ml, p=0.190; Il-10 2.42 ± 1.04pg/ml *v* 1.68 ± 0.19pg/ml, p=0.613). There was a significant inverse relationship of both total and bio-available testosterone with Il-1β (r_S=-0.262, p=0.024; r_S=-0.283, p=0.015), but not with other cytokines.
Conclusion: In men with coronary artery disease, low testosterone levels are associated with pro-inflammatory cytokine activation. Whether this represents cause or effect is unclear but the data may support a rationale for androgen replacement therapy in men with coronary artery disease.

1050-103 Prevalence of Hypogonadism in Men With Coronary Artery Disease

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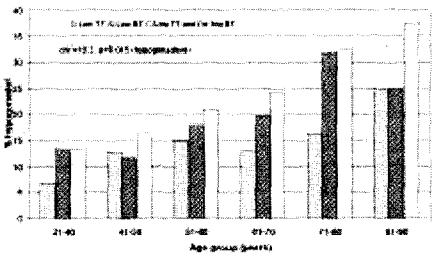
Background: Low serum testosterone level has been associated with numerous risk factors for coronary artery disease (CAD) and men with CAD have lower androgen levels than controls. Testosterone administration has a beneficial effect on various coronary risk factors and has been shown to reduce symptoms and ischaemia in men with angina, with greatest effect in hypogonadal men. Men with CAD therefore represent a population prone to testosterone deficiency who may especially benefit from hormone treatment. The purpose of this study was to determine the size of the problem. **Methods:** Blood samples were taken between 0800 and 0930hours from 900 men with proven CAD (≥ 70% stenosis in ≥ 1 epicardial coronary artery). 69 subjects with evidence of inflammation or elevated C-reactive protein were excluded. Serum levels of total (TT) and bio-available testosterone (BT) were measured in the remaining 831. Hypogonadism was defined as TT ≤ 7.5nmol/L and / or BT ≤ 2.5nmol/L. **Results:** TT was low in 117 subjects (14.1%). BT was low in 165 (19.9%). 194 had low TT and / or BT. The prevalence of hypogonadism therefore was 23.4%. It was more frequent in the obese (BMI>30) (33.3% *v* 19.1%, χ^2=15.8, p<0.0001) and less frequent in smokers (13.8% *v* 24.7%, χ^2=5.5, p=0.02). There was a significant relationship of hypogonadism with age (figure).



Conclusion: Using strict criteria, nearly a quarter of men with significant CAD are hypogonadal. Further trials are required to determine the benefits and safety of hormone replacement in these patients.

1050-104 Which Features of the Metabolic Syndrome Predict the Presence of Angiographic Coronary Artery Disease?

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Background: The metabolic syndrome (MS), a cluster of vascular risk factors, is growing in prevalence. The Adult Treatment Panel III Guidelines provide a uniform clinical definition of MS but offer no information about the individual and combined predictive value (PV) of its components for CAD.
Methods: We tested the PV of the MS and its components for CAD in a consecutive series of consenting, prospectively entered subjects undergoing coronary angiography for suspected cardiac disease. Acute MI at presentation was excluded. Components of the MS were assessed at the time of study entry (angiography) and included: 1) fasting glucose (FG) ≥110 mg/dL, 2) triglyceride (TG) ≥150 mg/dL, 3) high density lipoprotein cholesterol (HDL) <40 mg/dL in men or <50 mg/dL in women, and 4) systolic blood pressure (SBP) ≥130 and/or diastolic (D) BP ≥85 mmHg. MS was defined as ≥3 features. Waist circumference was not captured in the database, so body mass index (BMI; >27 kg/m2) was explored as a surrogate fifth measure. Angiographic assessment was